REMARKS

The Amendments

The claims are amended to add a proviso on the definition of $\mathbf{R^5}$ and **B** for the reasons discussed below. Support for the proviso is evident from the disclosure and original claims since the groups excluded by the proviso are specifically mentioned as optional groups.

Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Restriction Requirement

Applicants confirm their election with traverse of Group I, claims 1-19 and 25-27, pursuant to the Restriction requirement. Applicants also confirm their election with traverse of the species of compound #4028 shown in Table 4, page 133, of the specification. Applicants reserve the right to file one or more divisional applications directed to the non-elected subject matter.

Applicants respectfully traverse the restriction requirement between Groups I and II for the following reasons. The Office action alleges that the two groups do not relate to a single general inventive concept because they do not have the same or corresponding technical features. As proof thereof, the Office action refers to the Scola et al. reference. The instant claims, however, have been amended, as discussed below, to distinguish Scola. Thus, the basis is believed to not apply.

Further, applicants note the statement in the Office action that the method claims 20 and 23 are drawn to "various" uses of the products. Applicants respectfully disagree. All the methods of use derive from the use of the compounds to treat hepatitis C infection. Thus, applicants do not consider the compounds to be disclosed for "various" uses, to the extent that term is used to suggest the compounds have distinct sets of properties. Accordingly, restriction is not supported on the basis that the compounds are taught for use in materially different methods.

For all of the above reasons, the restriction requirement should be withdrawn in full.

Applicants note the comment in the Office Action regarding rejoinder. Should the restriction be maintained, applicants urge that the method claims are subject to rejoinder.

Regarding the Election of Species requirement, applicants hereby traverse the requirement to the extent it is effectively considered as a restriction among differing groups of compounds. Applicants submit that claim 1 provides a proper Markush claim (for the reasons discussed below) and should be examined pursuant to Markush practice. Under such practice, should no prior art be found which renders the invention of the elected species unpatentable, the search of the remainder of the generic claim(s) should be continued in the same application. The Office action states (at page 3, second paragraph) that should no prior art be found which renders the invention of the elected species unpatentable, the search of the remainder of the generic claim(s) will be continued in the same application. But the Office action also alleges that the generic claims lack unity of invention. Applicants urge that generic claim 1 does not lack unity of invention and seek confirmation that the claim will be examined according to Markush practice. If not, applicants urge an explanation of why restriction within the generic claim 1 is warranted.

Claim 1 is a proper Markush group. A Markush claim **can** contain independent and distinct inventions such that a prior art reference anticipating the claim with respect to one member would not render the claim obvious with respect to another member. The PTO's own rules on this matter set forth in M.P.E.P. §803.02 specifically state that:

> "A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. §103 with respect to the other member(s)."

This section of the M.P.E.P. makes clear that such a claim is a proper Markush claim and should be examined in accordance with Markush practice. Applicants request that, should the species election be considered as a restriction (to the extent requiring multiple applications to cover the genus), authority be cited as to why this section of the M.P.E.P. is not applicable. Furthermore, M.P.E.P. §2173.05(h) discusses types of improper Markush claims and applicants' claims are not of the type indicated to be improper therein. All compounds encompassed by instant claim 1 have a common structural core which is shown by the detailed formula (I) of claim 1 and exhibit a community of specific properties for treating hepatitis C infection, as discussed, for example, at page 1, lines 5-9, and page 8, line 5, to page 9, line 15, of the disclosure, for example. As discussed above, contrary to the allegation in the Office action, the compounds are not disclosed as having "various uses." All the uses relate to the specific property of the compounds for treating hepatitis C infection. Thus, claim 1 meets the requirement for Unity of Invention and as a proper Markush claim.

In any event, applicants encourage examination of the broadest possible scope of invention indicated by the elected species.

The Rejection under 35 U.S.C. §112, first paragraph

The rejection of claims 1-19 and 25-26 under 35 U.S.C. §112, first paragraph, for lack of enablement, is respectfully traversed.

Applicants submit that the original disclosure, taken in light of the knowledge of one of ordinary skill in the art, provides adequate teachings for one of ordinary skill in the art to make and use the claimed invention without undue experimentation. However, applicants submit herewith a Declaration under 37 C.F.R. §1.132 which additionally evidences the properties of representative compounds according to the claimed invention which support that they would be useful for the intended use described in the specification, e.g., to treat HCV infection.

Initially, applicants urge that the PTO has not met its initial burden of proof to assert lack of enablement. In order to support a rejection under 35 U.S.C. §112, first paragraph, for lack of enablement, the burden lies first with the PTO to provide evidence or objective reasoning substantiating the allegation that the enabling disclosure is not commensurate in scope with the claims. See, e.g., MPEP §2164.04 citing In re Marzocchi et al., 169 USPQ 367 (CCPA 1971), which states:

> ".. a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein..",

and further,

> "..it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a

> supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." (emphasis original).

Applicants' specification provides a teaching of how to use the claimed compounds which is commensurate in scope with the claims. See, e.g., page 8, line 5, to page 9, line 15, wherein the uses of the compounds are described as applicable to the full scope of compounds of formula (I). This disclosure "*must* be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein." The Office action does not set forth any reason to doubt these statements of the inventors in the specification. Further, the Office action fails to explain "*why* it doubts the truth or accuracy" of the inventors' statements of use in the specification. Absent any such reason or explanation for doubting the truth or accuracy of the inventors' disclosure, the PTO's initial burden is not met and the rejection should be withdrawn, at least for this reason.

Regarding the discussion of the factors a) – f) in the Office action, applicants have the following comments. However, regardless of these factors, the PTO has still not met the initial burden of proof to support the rejection.

The Office action states that determining if a particular compound within the claimed scope would be active would require making the compound and subjecting it to the NS3-NS4A protease assay. The Office action states that such would require a "large amount" of experimentation. However, the requirement of a large amount of experimentation does not equate to **undue** experimentation or lack of enablement. Where the experimentation required is merely routine experimentation to one of ordinary skill in the art, it is not undue experimentation

and does not support a case for lack of enablement. See, e.g., In re Wands, 858 F.2d at 736-37, 8 USPQ2d at 1404, stating: "Enablement is not precluded by the necessity for some experimentation ... . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation'." See also Ex parte Jackson, 217 USPQ 804 (Bd. Pat. App. 1982), stating: "The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. ... The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed." As the Office action implicitly acknowledges, the specification here provides the guidance necessary to one of ordinary skill in the art to proceed with the required experimentation, i.e., the specification identifies the assays necessary to determine the activity of the compounds; see, e.g., page 115, line 20, to page 116, line 23. The specification also provides an adequate amount of direction on the manner of administration of the compounds (see, e.g., page 62, line 12, to page 66, line 8) and a large amount of detail and examples on how to make the compounds (see, e.g., page 66, line 10, to page 115, line 18).

The Office action states that the specification merely indicates an intent to make and use compounds limited by the variables recited at the top of page 6 of the Office action. However, a review of Tables 1-6 (pages 117-137) of the specification makes clear that applicants made compounds which a much larger variety of variables. Also, the specification states (page 116,

lines 10-14) that many of the compounds shown in those tables "were found to have IC50 values below 1 μM in the NS3-NS4A protease assay of Example 7." Representative compounds were also tested in the cell-based luciferase reporter HCV RNA replication assay of Example 8. Thus, the compounds were tested to show their activity.

To further evidence the activity of a representative sampling of the compounds, applicants have submitted a Declaration under 37 C.F.R. §1.132. The declaration provides data on the cell-based luciferase reporter HCV RNA replication assay for compounds according to the claimed invention. A representative group of compounds were selected which show a variety of variables on the R^1, R^2, R^4 and R^6 substituents of applicants' general formula (I). The results in the table on page 4 show that the compounds exhibited cell-based activity in the assay despite the difference in variables.

The Office action further indicates that lack of enablement is evidenced because the use of applicants' compounds is based on their physiological effect and that such use is inherently unpredictable. Applicants respectfully disagree that any use related to physiological activity is necessarily unpredictable to the extent of supporting lack of enablement. There is no evidence on the record to support such a statement. The Office action alleges that there is no reasonable basis to assume the scope of claimed compounds would share the same class of biological properties. However, as discussed above, applicants have provided the inventors' disclosure stating such use and a representative amount of evidence to support the disclosure. In view thereof, the PTO has provided no evidence to refute the inventors' statements or the representative assay data. The burden of proof lies with the PTO to make a case for non-enablement. The Office action alleges that the compounds are chemically non-equivalent but there is also no basis for this statement.

Clearly, the compounds do share a large degree of structural similarity as shown by the general structural formula (I) of claim 1. Further, a representative amount of these compounds – with varying substitutents – have been shown to exhibit a shared biological activity in the assays. There is no evidence on the record to refute that such activity derives from the shared structural aspects of the compounds shown by applicants' formula (I). The standard for enablement is not absolute predictability but only reasonable expectation of success; see In re Wright, 999 F.2d 1557, 27 USPQ2d 1510,1512 (Fed.Cir. 1993). Applicants urge based on the above discussion that a reasonable expectation of success is supported on the record as a whole and that no evidence is provided by the PTO to indicate otherwise.

For all of the above reasons, applicants urge that applicants' disclosure provides one of ordinary skill in the art – considering the knowledge available in the art at the time of the invention – adequate teachings to make and use the claimed invention using only routine experimentation which is described in the disclosure. Thus, the instant claims are enabled and the rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

The Rejections for Obviousness-type Double Patenting and under 35 U.S.C. §102(e) and §103 over US Pub. No. 2005/0020503

The rejections of claims 1-19 and 25-26 over U.S. Pub. No. 2005/0020503 (Ser. No. 10/850,101) (" the '101 application"), provisionally for obviousness-type double patenting, for anticipation under 35 U.S.C. §102(e) and for obviousness under 35 U.S.C. §103, are respectfully traversed.

Applicants respectfully note that, contrary to the statement in the Office action, the

compounds defined by the instant claims do not overlap in scope with the compounds claimed or disclosed in the '101 application. Specifically, the proviso at the end of instant claim 1 excludes the compounds having the substitution pattern described in the '101 application. This proviso was in the original claims and disclosure and was added for the purpose of excluding the scope of the compounds claimed and disclosed in the '101 application.

Absent any overlap in the claims' scope, there is clearly no anticipation and no support for the rejection under 35 U.S.C. §102(e). Further, applicants urge that there is no support for the obviousness-type double patenting or obviousness rejections. As noted above, the instant claims do not cover the compounds substituted as described in the '101 application. Furthermore, there is no suggestion from the '101 application to modify the '101 application compounds to arrive at the compounds of the instant claims. Thus, the provisional obviousness-type double patenting rejection and the rejection under 35 U.S.C. §103 should also be withdrawn.

The Rejections under 35 U.S.C. §102 and §103 over Scola

The rejections of claims 1-19 and 25-26 over Scola (U.S. Pat. No. 7,132,504), for anticipation under 35 U.S.C. §102(e) and for obviousness under 35 U.S.C. §103, are respectfully traversed.

Claim 1 (upon which all other claims ultimately depend) has been amended above to address the Scola reference. The proviso excludes the compounds which Scola specifically exemplifies or otherwise specifically defines.

Scola provides a broad generic formula (I) defined at cols. 2-3. However, the only compounds specifically exemplified or otherwise specifically defined by Scola are those where

the B group of Scola is –C(=O)-O-alkyl with alkyl being methyl or tert-butyl. See the disclosure at col. 12, lines 2-3, and the Examples at cols. 57-72. Of the 26 compounds Scola discloses having a specific B group, in everyone of them B is –C(=O)-O-alkyl with alkyl being methyl or tert-butyl.

In view of the above, Scola fails to anticipate the claimed invention. Scola provides no specific embodiment or specific evidence to suggest that the reference inventors were in possession of an embodiment meeting the elements of the instant claims. A mere broad generic disclosure without any specific direction as to the specific element(s) necessary to provide an anticipation is not an anticipatory disclosure. In other words, such a broad generic disclosure does not "describe" an embodiment therein in accordance with 35 U.S.C. §102. See In re Kollman et al, 201 USPQ 193 (CCPA 1979). If such a reference were anticipatory, it would not be possible to prove nonobviousness for selection inventions within a generic disclosure. Such is not the state of the law. Accordingly, at least the rejection under 35 U.S.C. §102 over Scola should be withdrawn.

Additionally, applicants urge that – despite its broad generic formula – Scola does not provide a disclosure which fairly suggests the claimed invention and, thus, does not render the claimed invention obvious under 35 U.S.C. §103. As was clearly set forth in In re Jones, 21 USPQ 2d 1941 (Fed. Cir. 1992), it is not the law that ".. regardless of how broad, a disclosure of a chemical genus renders obvious any species which happens to fall within it." Instead, the disclosure must be considered as a whole as to whether it fairly suggests the claimed invention to one of ordinary skill in the art; see also In re Baird, 29 USPQ2d 1550 (Fed. Cir. 1994). As in Jones and Baird, the reference provided a generic disclosure which encompassed a very large

number of compounds, there were no specific teachings in the reference to suggest the specific selection of variables necessary to arrive at the claimed compounds and, in fact, the reference indicated a preference for compounds distinct from the claimed compounds. In view of the preferences and examples disclosed in Scola, applicants urge that the facts are analogous to Jones and Baird. Therefore, as the Courts concluded in Jones and Baird, the reference does not fairly suggest the claimed compounds and, thus, does not render the claimed invention prima facie obvious. Accordingly, the rejection under 35 U.S.C. §103 over Scola should also be withdrawn.

Regarding claim 11, additional basis for nonobviousness is provided. Scola fails to give any suggestion of compounds having the type of heterocyclic group described for the R^2 substituent in this claim.

Claim 27

Applicants note that claim 27 is not subject to any of the grounds of rejection, however, it is listed as a rejected claim in the cover sheet of the Office Action. It would appear that the claim should be allowable but clarification is requested.

It is submitted that the claims are in condition for allowance. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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